I. AMENDMENT

IN THE SPECIFICATION

• Please replace the paragraph beginning at page 1, line 5, with the following rewritten paragraph:

-- This application claims priority from U.S. Application Serial No. 60/209,584, filed June 6, 2000, which application is related to ~~a continuation-in-part of co-pending~~ U.S. Application Serial No. 08/554,840, filed November 7, 1995, and issued as U.S. Patent No. 6,001,358 on December 14, 1999, the entirety of which are incorporated herein by reference. --

• Please replace the paragraph beginning at page 9, line 15, with the following rewritten paragraph:

-- In a commonly assigned application, Serial No. 07/912,292, "Primatized"® antibodies are disclosed which contain human constant and Old World monkey variable regions. These Primatized® antibodies are well tolerated in humans given their low or weak immunogenicity. --

• Please replace the four paragraphs numbered (1) to (4) beginning at page 13, line 7, with the following rewritten paragraphs:

-- (1) DIVMTQSPSFLSASVGDRVTITC KASQNVITAVA WYQQKPGKSPKLLIY SASNRYT GVPDRFSGSGSGTDFTLTISSLQPEDFADYFC QQYNSYPYT FGGGTKLEIK [SEQ ID NO:1];

(2) DIVMTQSPDSLAVSLGERATINC KASQNVITAVA WYQQKPGQSPKLLIY SASNRYT GVPDRFSGSGSGTDFTLTISSLQAEDVADYFC QQYNSYPYT FGGGTKLEIK [SEQ ID NO:2];

(3) DIVMTQSPSFMSTSVGDRVTITC KASQNVITAVA WYQQKPGKSPKLLIY SASNRYT GVPDRFSGSGSGTDFTLTISSMQPEDFADYFC QQYNSYPYT FGGGTKLEIK [SEQ ID NO:3];

(4) DIVMTQSPDSMATSLGERVTINC KASQNVITAVA WYQQKPGQSPKLLIY SASNRYT GVPDRFSGSGSGTDFTLTISSMQAEDVADYFC QQYNSYPYT FGGGTKLEIK [SEQ ID NO:4] - -

• Please replace the four paragraphs numbered (1) to (4) beginning at page 14, line 8, with the following rewritten paragraphs:

- - (1) EVQLQESGPGLVKPSETLSLTCTVSGDSIT NGFWI WIRKPPGNKLEYMG YISYSGSTYYNPSLKS RISISRDTSKNQFSLKLSSVTAADTGVYYCAC RSYGRTPYYFDF WGQGTTLTVSS [SEQ ID NO:5];

(2) EVQLQESGPGLVKPSQTLSLTCTVSGDSIT NGFWI WIRKHPGNKLEYMG YISYSGSTYYNPSLKS RISISRDTSKNQFSLKLSSVTAADTGVYYCAC RSYGRTPYYFDF WGQGTTLTVSS [SEQ ID NO:6];

(3) EVQLQESGPGLVKPSQTLSLTCAVSGDSIT NGFWI WIRKHPGNKLEYMG YISYSGSTYYNPSLKS RISISRDTSNNQFSLNLNSVTRADTGVYYCAC RSYGRTPYYFDF WGQGTTLTVSS [SEQ ID NO:7];

(4) EVQLQESGPGLVKPSETLSLTCAVYGDSIT NGFWI WIRKPPGNKLEYMG YISYSGSTYYNPSLKS RISISRDTSKNQFYLKLSSVTAADTGVYYCAC RSYGRTPYYFDF WGQGTTLTVSS [SEQ ID NO:8] - -

• Please replace the four paragraphs numbered (1) to (4) beginning at page 15, line 31, with the following rewritten paragraphs:

- - (1) DIVMTQSPSFLSASVGDRVTITC KASQNVITAVA WYQQKPGKSPKLLIY SASNRYT GVPDRFSGSGSGTDFTLTISSLQPEDFADYFC QQYNSYPYT FGGGTKLEIK [SEQ ID NO:1];

(2) DIVMTQSPDSLAVSLGERATINC KASQNVITAVA WYQQKPGQSPKLLIY SASNRYT GVPDRFSGSGSGTDFTLTISSLQAEDVADYFC QQYNSYPYT FGGGTKLEIK [SEQ ID NO:2];

(3) DIVMTQSPSFMSTSVGDRVTITC KASQNVITAVA WYQQKPGKSPKLLIY SASNRYT GVPDRFSGSGSGTDFTLTISSMQPEDFADYFC QQYNSYPYT FGGGTKLEIK [SEQ ID NO:3];

(4) DIVMTQSPDSMATSLGERVTINC KASQNVITAVA WYQQKPGQSPKLLIY SASNRYT GVPDRFSGSGSGTDFTLTISSMQAEDVADYFC QQYNSYPYT FGGGTKLEIK [SEQ ID NO:4] - -

• Please replace the four paragraphs numbered (1) to (4) beginning at page 16, line 21, with the following rewritten paragraphs:

- - (1) EVQLQESGPGLVKPSETLSLTCTVSGDSIT NGFWI WIRKPPGNKLEYMG YISYSGSTYYNPSLKS RISISRDTSKNQFSLKLSSVTAADTGVYYCAC RSYGRTPYYFDF WGQGTTLTVSS [SEQ ID NO:5];

(2) EVQLQESGPGLVKPSQTLSLTCTVSGDSIT NGFWI WIRKHPGNKLEYMG YISYSGSTYYNPSLKS RISISRDTSKNQFSLKLSSVTAADTGVYYCAC RSYGRTPYYFDF WGQGTTLTVSS [SEQ ID NO:6];

(3) EVQLQESGPGLVKPSQTLSLTCAVSGDSIT NGFWI WIRKHPGNKLEYMG YISYSGSTYYNPSLKS RISISRDTSNNQFSLNLNSVTRADTGVYYCAC RSYGRTPYYFDF WGQGTTLTVSS [SEQ ID NO:7];

(4) EVQLQESGPGLVKPSETLSLTCAVYGDSIT NGFWI WIRKPPGNKLEYMG YISYSGSTYYNPSLKS RISISRDTSKNQFYLKLSSVTAADTGVYYCAC RSYGRTPYYFDF WGQGTTLTVSS [SEQ ID NO:8] - -

• Please replace the five paragraphs describing figures 4-8 beginning at page 19, line 11, with the following rewritten paragraphs:

- - **Figure 4** [SEQ ID NO:24] contains the amino acid sequence and DNA sequence corresponding to a preferred humanized variable light sequence (including the

complementarity determining regions) referred to as VL#1 or preferred humanized variable light sequence (1).

Figure 5 [SEQ ID NO:25] contains the amino acid and DNA sequence corresponding to a preferred humanized variable ligand sequence (including the complementarity determining regions) referred to as VL#2 or preferred humanized variable light sequence (2).

Figure 6 [SEQ ID NO:26] contains the amino acid and DNA sequence corresponding to a preferred humanized variable heavy sequence (including the complementarity determining regions) referred to as VH#1 of preferred humanized variable heavy sequence (1).

Figure 7 [SEQ ID NO:27] contains the amino acid and DNA sequence of the variable light sequence of 24-31 (non-humanized).

Figure 8 [SEQ ID NO:28] contains the amino acid and DNA sequence of the variable heavy sequence of 24-31 (non-humanized). - -

- Please replace the paragraph beginning at page 25, line 4, with the following rewritten paragraph:

- - The cloning of the variable regions of 24-31 (described in detail in the examples *infra*) resulted in the identification of the V_L and V_H and sequences utilized by the 24-31 antibody respectively shown in **Figure 7** [SEQ ID NO:27] and **Figure 8** [SEQ ID NO:28]. After sequencing, the variable regions were then humanized. As noted, this was effected substantially according to the method of Padlan (1994) (Id.), incorporated by reference *supra*.
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Please replace the paragraph beginning at page 25, line 15, with the following rewritten paragraph:

- - More specifically, the 24-31 V_K and V_H sequences set forth in **Figures 7** [SEQ ID NO:27] and **Figure 8** [SEQ ID NO:28] were humanized by comparison to human antibodies of reported sequence, which are referred to as "templates." - -

- Please replace the paragraph beginning at page 26, line 7, with the following rewritten paragraph:

- - This methodology resulted in the following preferred humanized V_L and V_H heavy sequences derived from the 24-31 antibody which are set forth below in **Table 1** [SEQ ID NOs:1-4] and **Table 2** [SEQ ID NOs:5-8]. As discussed above, the invention further embraces equivalents and variants of these preferred humanized sequences, e.g., those containing one or more conservative amino acid substitutions which do not substantially affect gp39 binding. The complementarity determining regions are identified in **Figures 7** [SEQ ID NO:27] and **Figure 8** [SEQ ID NO:28] which contain the entire variable heavy and light chain CDR sequences of the parent (non-humanized) 24-31 antibody. - -

- Please replace the paragraph beginning at page 29, line 7, with the following rewritten paragraph:

- - So as to better describe the subject humanized 24-31, V_H and V_L sequences, the preferred humanized framework sequences [SEQ ID NOS:. 9-21] are also set forth in **Table 3** below, which compares these sequences to the template human variable heavy and light framework sequences, i.e., human DEN VK1, Human o12/V36 germline, human LEN VKIV, human 58p2, human Z18320, and human 3d75d as well as to the unhumanized murine 24-31 V_H and V_L framework sequences. - -

Please replace the paragraph beginning at page 32, line 6, with the following rewritten paragraph:

-- In order to produce humanized antibodies, DNA sequences are synthesized which encode for the afore-identified humanized V_L and V_H sequences. As noted, taking into account these four humanized V_L sequences, and four humanized V_H sequences, there are 16 potential humanized antigen combining sites which may be synthesized. Also, there are even more potential humanized antigen combining sites taking into account the potential substitution of residues 34, 43, 44 and 68 of the humanized V_H and residue 85 of the humanized V_L by other amino acid residues and/or the potential incorporation of conservative substitution mutations. Two of the preferred humanized variable light sequences (1) and (2) and a preferred humanized variable heavy sequence (1) including the complementarity determining regions and corresponding DNA sequences are set forth in **Figures 4, 5, and 6** [SEQ ID NOS:. 24-26], respectively. --

• Please replace the paragraph beginning at page 44, line 18, with the following rewritten paragraph:

-- **b. PCR amplification ~~Of~~ of V_k and V_H cDNA.** 24-31 and NS1 cDNA were amplified by PCR using a panel of 5' primers specific for V_k or V_H leader sequences in combination with 3' constant region primers. The panel of 5' V_H primers are identical to those described by Jones and Bendig (Bio/Technol., 9:88 (1991); Errata, Bio/Technol., 9:579 (1991)). The panel of 5' V_k primers (Jones et al., (id.)) were modified to convert the Sal I cloning site recognition sequences (GTCGAC) into Bgl II recognition sequences (AGATCT) to facilitate the cloning of the amplified gene segments into IDEC's N5KG1 expression vector (See **Figure 1**). The 3' V_k and V_H primers contain a Bsi WI cloning site sequence at amino acid positions 108-109 (numbering according to Kabat et al., "Sequences of Proteins of Immunological Interest," 5th Ed., NIH (1991)) and a Nhe I cloning site sequence at positions 114-115, respectively, and have the following sequences:
TGCAGCATCCGTACGTTTGATTCCAGCTT (C_k) [SEQ ID NO:22] and